

PATIENT'S ASSISTANCE AND SAFETY QUALITY MANAGEMENT IN ANTICOAGULANT THERAPY FOR THE ORTHOPEDIC PATIENT

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ABSTRACT

It refers to an integrative review study around the records on anticoagulant medicaments used in orthopedic patients and about what is said in terms of safety of the patient using this therapy. Collection was developed using the electronic databases PUBMED, SCIELO, LILACS and WEB OF SCIENCE. Search on the online databases was conducted using the following terms as MeSH: Patient safety, anticoagulants and orthopedics. The inclusion criteria were to opt for publications with complete texts using English, Portuguese and Spanish languages and dated on the last 5 years. After reading, selecting and excluding, 48 scientific productions were obtained. The material selected through the electronic databases was organized through direct observation and originated recovery of data about the subject and its discussion. It is expected that the results of this study stimulate initiatives by healthcare professionals, searching to promote the healthcare assistance quality and orthopedics patient safety binomial.

INTRODUCTION

It is known that anticoagulants are classified as potentially dangerous medicaments, considered to be of high vigilance by the National Sanitary Vigilance Agency (ANVISA – *Agência Nacional de Vigilância Sanitária*) and to cause important adverse events when used in non-appropriate manner, even leading, amongst others, to a severe clinical denouement: hemorrhage.

The patient safety improvement and health care assistance quality issue has received special attention worldwide. In this context, ANVISA has instituted an ordered sequence of activities aimed towards patient safety and quality in healthcare services.

In October 2004, the World Health Organization (WHO) launched the World Alliance for Patient Safety and identified processes that could contribute with this strategy. The main goal of this initiative is to avoid damage to the patient, reducing the negative consequences of treatment performed unsafely.

The anticoagulants (ATG) are medicaments that aim to decrease the possibility of clots forming inside the heart and blood vessels, preventing their obstruction. Usually, blood stays in liquid form as it maintains contact with the internal surfaces of the heart and blood vessels. That happens due to a complex physical-chemical balance, where forces are cancelled, which on one side favors coagulation and, on the other side, anticoagulation. When in contact with any other type of biological surface or different kind of surface, the balance changes and blood tends to coagulate (GUIMARÃES, 2007).

Evidence shows that the main complication of ATG use is bleeding and that this process can be evolutional, potentially with larger bleedings in compartments such as the intracranial and retroperitoneal, for example, which can be fatal. An example of AE (Adverse Event) to the use of ATG is the Hemorrhagic Cerebrovascular Accident (CVA), which can lead to death or make the stricken individual's life very unfavorable due to the sequelae. Another example of AE manifested through minor bleeding is anemia, which normally is caused by micro gastrointestinal hemorrhages. However, in cases where therapy with this group of medicaments is indicated, it is important to consider the potential benefit in preventing or treating thromboembolic events (WILT, 1995).

In other words, it is indispensable that the health care professionals are able to associate the anticoagulant therapy with the orthopedics patient's safety in order to promote quality and damage free assistance. In this sense, the goal of this study was to perform a review study on the online databases around the records about anticoagulant medicaments used in orthopedics patients and what is said in terms of safety of patients using this therapy.

Materials and Methods

This study is characterized as an integrative review. Integrative reviews are the broadest type of review research, for they allow the simultaneous inclusion of experimental and non-experimental researches, combination of empiric and theoretic literature and incorporation of a big range of purposes: definition of concepts, theory reviews, evidence reviews and analysis of methodological questions for a specific subject (WHITTEMORE, 2005).

The elaboration of an integrative review occurs in six distinct phases: Identification of subject and research questions, Sampling or literature research, Categorization of studies, Evaluation of studies included in the bibliographic review, Interpretation of results and Synthesis of knowledge evidenced in the analyzed articles or presentation of the integrative review (BROOME, 2000).

The search occurred in April 2014 and was updated in November 2014. The collection was developed using the electronic databases PUBMED, Scientific Electronic Library Online – SCIELO, Literatura Latino-Americana e do Caribe em Ciências da Saúde (*Latin-American and Caribbean Literature in Health Sciences*) – LILACS and WEB OF SCIENCE.

Search on the online databases was conducted using the following terms as Medical Subject Headings (MeSH): Patient safety, anticoagulants and orthopedics. The inclusion criteria used were to opt for publications with complete texts, using English, Portuguese and Spanish languages and dated on the last 5 years.

After reading, selecting and excluding, 48 scientific productions were obtained. The material selected through the electronic databases was organized via direct observation and, subsequently, discussed.

RESULTS

The table below shows the distribution of the material found according to the databases used for research and the MeSH associations.

MeSH	PUBMED	SCIELO	LILACS	Web of Science
Patient safety AND Anticoagulants AND Orthopedics	1	0	0	0
Patient safety AND Anticoagulants OR Orthopedics	236	74	866	375
Patient safety OR Anticoagulants AND Orthopedics	651	0	0	0
Patient safety OR Anticoagulants OR Orthopedics	1694	3201	1030	3920

Table 1- Quantitative description of the material found in the electronic databases PUBMED, SCIELO, LILACS and WEB OF SCIENCE. Source: Author’s property.

After concluding the search, it was possible to observe that the MeSH association to show the best refinement was: Patient safety “AND” Anticoagulants “OR” Orthopedics, which was chosen for proceeding with the collection and extraction of the significant and indispensable variables that composed the records around anticoagulant therapy to the orthopedic patient.

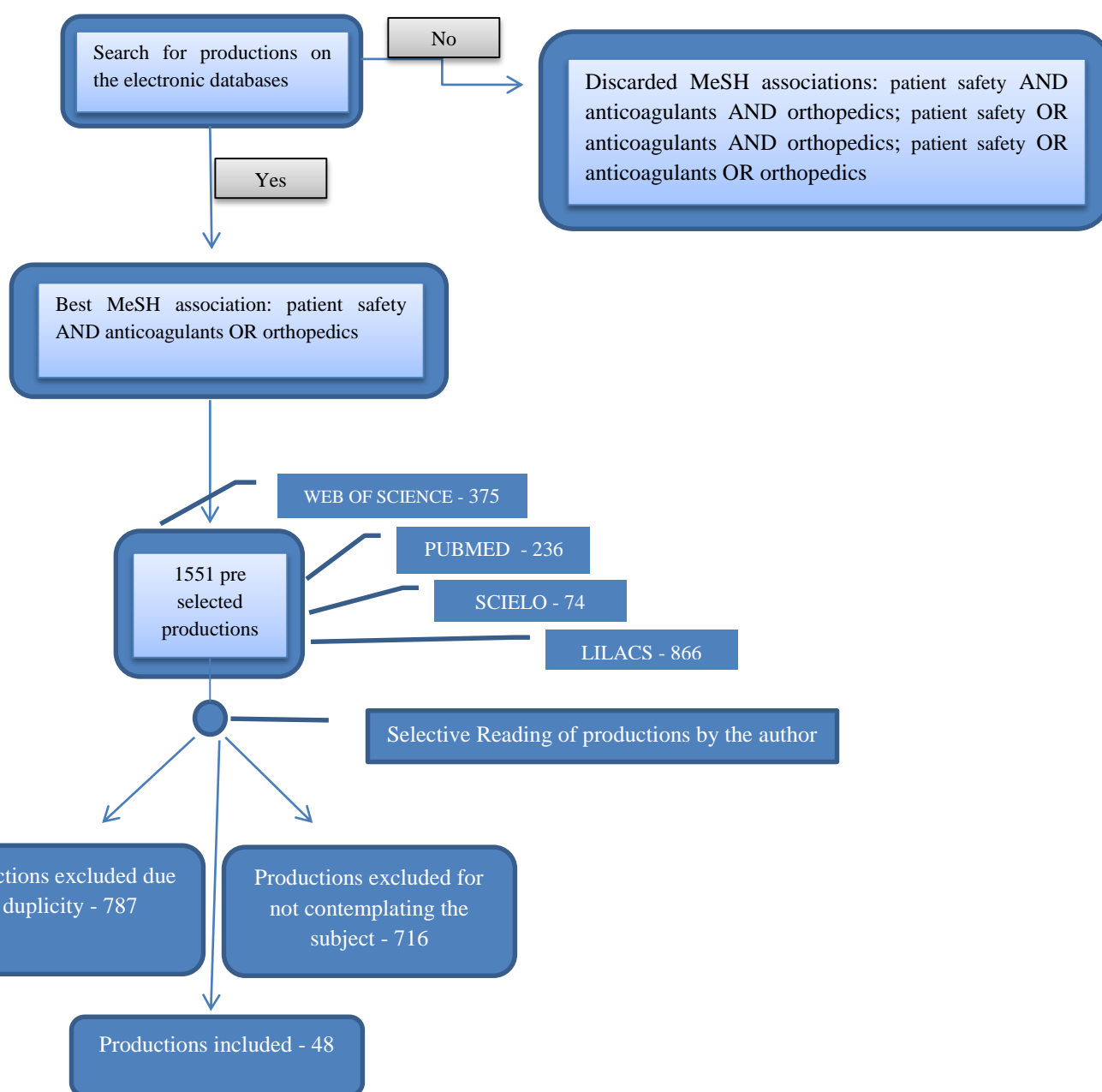


Figure 1- Flowchart for search and selection of scientific productions. Source: Author’s property.

RECOVERING THE INFORMATION CONTAINED IN THE ANALYZED PRODUCTIONS AND DISCUSSION***1. Anticoagulants – Main Adverse Events and the physiopathology of the most severe clinical denouement - hemorrhage***

Over the last 10 years, an exponential growth in the development of anticoagulant agents for clinical use was observed. Scientific literature has increased with new evidence of antithrombotic drugs application, with innovative medicaments, already approved by ANVISA for use in Brazil. This brings alternatives to anticoagulant therapy, however, it imposes recommendations as well as specific restrictions and risks associated to each medicament, that must be observed before using them and during the defined therapy. In this sense, with the development of new and modern medications, patient safety began to be more valued, including more attention to risks of bleeding (SBC, 2013).

It is important to clarify that, didactically, the antithrombotic medicaments are divided into antiplatelet agents and anticoagulants. In order to further this study, the anticoagulant medicaments most used in the market and hospital institutions will be approached, since the target audience are orthopedic patients that, mostly, make use of this class of medicament for TVP and TEP prophylaxis.

Following what is most current today, in terms of anticoagulant medicaments, it is possible to divide them in groups: Unfractionated Heparin; Low Molecular Weight Heparin; Coumarin and Indandiones; Xa Factor Inhibitors and Thrombin Inhibitors. Sodium heparin is the example from the group of Unfractionated Heparin. As examples of Low Weight Heparins, we have enoxaparin, most currently used medicament on the prophylaxis for Venous Thromboembolism (VTE), dalteparin, ardeparin, tinzaparin and danaparoid. The examples of Coumarin and Indandiones are warfarin, acenocoumarol, fenindione and phenprocoumon. The medicaments considered to be Xa Factor Inhibitors are fondaparinux, rivaroxaban and apixaban and, lastly, the ones who comprise the group of Thrombin Inhibitors are bivalirudin, dabigatran, argatroban, desirudin and lepirudin (SBC, 2013).

Regarding the administration form, it can be one of three types: oral, intravenous or subcutaneous. The intravenous are drugs for exclusive use in hospitals. The most used is sodium heparin. The subcutaneous are, currently, the most used in health institutions. Due to their safety and stability, they can also be administered at home, in case the patient or a relative has been prepared to do so. The Low Molecular Weight Heparin and its derivatives are used in this via of administration (Ex: Enoxaparin).

The oral ones have the extremely powerful effect of inhibiting the coagulation ability of the blood. They need rigorous care, because the ideal dosage may be difficult to be defined, needing constant laboratory control for its adjustment. When the dosage is not adequate, it may allow the formation of clots in the circulatory system or spontaneous bleedings, sometimes very severe. The most used group with this purpose is the Coumarin (Ex: Warfarin). Most recently, new modern oral drugs have been adopted, such as dabigatran (Pradaxa®) and rivaroxaban (Xarelto®), amongst others, however their use in Brazil is more observed on the private network, due to their high acquisition cost.

The most used anticoagulants in public hospitals, currently, are enoxaparin (Clexane®) and warfarin (Marevan®), as mentioned before. Usually, the enoxaparin is used in VTE prophylaxis, whereas warfarin is more observed as a clinical conduct for patients in treatment for TVP/TEP. Regarding the enoxaparin, it is possible to say it is a low molecular weight heparin. It is obtained through depolymerization of heparin and consequent decrease in molecular weight. It is more used currently for having a smaller risk of inducing bleeding, when compared to unfractionated heparin used in prophylaxis of TVP and its treatment. Normally, in patients with high risk of VTE, it is used a daily dose of 40mg for prophylaxis. For moderate risk, a 20mg/day dose can be used. Regarding warfarin, it is a medicament that presents a variable dosage for each person. Generally, most users reach a state of anticoagulation with 4 to 6mg/day. However, other people may need a smaller or bigger dosage (GUIMARÃES, 2007).

Warfarin begins to present anticoagulant effect within 24 hours after the first dose. However, full effect may take 3 to 5 days to occur. Most users reach a state of anticoagulation with a dose of 5mg/day, sometimes up to 7,5mg. Several foods and medications may interfere in the anticoagulant effect. That is why, in order to find the ideal dosage, it is necessary to perform a blood test – prothrombin time and partial thromboplastin (TAP and PTT with INR). During this period, in order to keep the patient away from the risk of forming clots, it may be necessary to associate the use of low molecular weight heparin (Clexane®) until TAP and PTT with INR reach the expected effect (GUIMARÃES, 2007).

ATG have high drug interaction with other drugs, and the main complication is hemorrhage. The annual average of fatal bleedings in patients using warfarin is 0.6%, of major bleeding is 3% and of major or minor bleeding is 9.6%. Comorbidities and age also contribute to the increase in risk of complications (LANDFELD, 1993).

It is worth highlighting the AE related to the use of anticoagulants. The example of the two most used medicaments in public health care institutions in Brazil was considered; enoxaparin, usually for prophylactic use and warfarin, for VTE clinical treatment use. The ones pointed out by Drugs, international reference website for medicament information, as possible with the use of ATG, are divided by systems, described as follows:

- 1- For enoxaparin: *Hematological* (hematoma, anemia, bruises, thrombocytopenia, thrombocytosis, increase in PTT and INR, hemarthrosis e retroperitoneal hematoma); *Hepatic* (elevation of the hepatic function markers); *Dermatological* (purple, rash and cutaneous vasculitis); *Respiratory* (acute lung edema, pneumonia e dyspnea); *Cardiovascular* (atrial fibrillation, myocardial failure, general edema and pericardial edema); *Gastrointestinal* (nausea and diarrhea); *Metabolic* (hyperkalemia, tissue hematoma and, rarely, cholesterol increase); *Genitourinary* (hematuria); *Nervous System* (mental confusion).
- 2- For warfarin: *Hematological* (hemorrhage, head ache, paresis, paresthesia, chest pain, abdominal, muscular or any other pain, dizziness, dyspnea, edema, hypotension, weakness, elevation in PTT and INR, platelets alteration); *Hepatic* (elevation of the hepatic function markers); *Dermatological* (purple, rash and cutaneous vasculitis); *Respiratory* (acute lung edema, pneumonia e dyspnea); *Cardiovascular* (atrial fibrillation, myocardial failure, general edema and pericardial edema); *Gastrointestinal* (nausea and diarrhea); *Metabolic* (hyperkalemia, tissue hematoma and, rarely, cholesterol increase); *Genitourinary* (hematuria); *Nervous System* (mental confusion).

It is necessary to observe that, according to Drugs, bleeding may result in hematoma, melena, hematuria, bruise, epistaxis and hematemesis, spontaneous intra spinal hematoma, gastrointestinal, ocular, intra-abdominal hemorrhage, hemopericardium, posttraumatic compartment syndrome and the most severe clinical denouement, cerebral hemorrhage. This information elucidates the need for the creation and implementation of mechanisms that promote patient safety, health care assistance quality, consequently, making less insidious the medication error and the occurrence of drug interaction, by the health care professional and the monitoring and early detection of any possible ADR.

Hemorrhage or bleeding is the loss of the circulatory system's blood. The initial cardiocirculatory system's response to acute blood loss is a compensatory mechanism, that is, cutaneous, muscular and visceral vasoconstriction occurs, in order to attempt to maintain blood flow to the kidneys, heart and brain, organs that are more important for life maintenance. An increase in heart rate also occurs to attempt to maintain cardiac debt. Thus, tachycardia is, many times, the first sign of hypovolemic shock. Since catecholamines provoke peripheral vascular resistance increase, diastolic pressure tends to increase, getting closer to systolic pressure. The liberation of other hormones in this phase makes the person extremely pale, with tachycardia and thread pulse, hard to palpate (PONTES-NETO, 2009).

Despite all this compensatory mechanism, there is a limit when, if exceeded, the organism begins to fail. Victims of traumas with important blood loss and delayed aid may have temporary tissue ischemia, with the liberation of substances typical to the anaerobe metabolism. With a longer time, lack of energy to maintain regular cell membrane and electric gradient occurs. The cell, not supporting the ischemia anymore, initiates the rupture of lysosomes and cell auto digestion. Without the reversion of the process, death, finally, occurs.

Receiving health assistance at the proper moment, blood volume is initially restored through saline solutions administered and the chances of the individual to recuperate are big, however, important sequelae may occur. Knowing the risks and developments of a major hemorrhagic episode, mechanisms must be implemented in order to avoid this denouement in health care assistance.

2. Adverse Drug Event, Adverse Drug Reaction, Drug Interaction and mistakes related to drug therapy: Clinical and economic consequences

Pharmacovigilance is one of fields of ANVISA, which performs activities related to the identification, evaluation, comprehension and prevention of AE or any possible issue related to medicaments. Among the goals of pharmacovigilance, it is possible to highlight detecting unknown ADRs and drug interaction; detecting the increase rate of unknown ADRs; identifying risk factors and possible development mechanisms of ADRs; estimating quantitative aspects of the benefit/risk analysis and disseminating information necessary to promote proper prescription and regulation of drugs, promoting rational and safe use of these products (BRASIL, 2011).

According to the World Health Organization (2009), an Adverse Drug Event is understood as any unwanted medical occurrence that occurs with a patient that has received a pharmaceutical product and that does not have necessarily an established causal relation with this treatment. An adverse event includes any unfavorable and

unintentional sign (abnormal laboratory findings, for example), symptoms, or disease temporarily associated with the medicament use, related or not to the medicament.

Adverse Drug Reaction (ADR) can be defined as any damaging and unintentional response to a medicament usually used at prophylaxis, diagnose or pathology treatment dosage or, still, for modification of physiological function, but not due to a medication error. It is important to highlight that, in order to be considered an ADR, there must be a causality relation between the sign/symptom and the medicament in question (EDWARDS, 2000).

Drug Interaction (DI) is the result of alteration of the pharmacological effects between two or more medicaments administered simultaneously, with the chance of resulting in increase or decrease in therapeutic efficiency or in AE caused by these, or still, the rise of new effects (BRASIL, 2010).

Medication error is understood as any avoidable event that, as a matter of fact or potentially, can lead to inadequate use of medicament. This concept implies that the inadequate use may or may not injure the patient. The error may be related to professional practice, Health Care products, procedures, communication problems, including prescription, labels, packages, names, preparation, dispensation, distribution, administration, education, monitoring and medicament use (NCCMERP, 2001).

The consequences of the broad use of medicaments has impact on clinical and economic ambits, reflecting on patient safety. And, despise the dramatic effects that organic changes arising from a vulnerability situation create on medicament response, pharmacologic intervention is, still, the most used for prophylaxis of thromboembolic events (SECOLI, 2010).

Medicaments have the possibility of solving several health issues, increasing life expectancy, eradicating certain diseases and minimizing suffering in individuals. However, they may cause damage and also contribute to the increase in health costs if used incorrectly or without proper control and/or lead to the occurrence of AE (SANTOS, 2010).

Harvard Medical Practice Study I and II, remarkable and pioneer in the area of patient safety, showed that AE related to assistance are common and unexpectedly high in North-American hospitals, resulting in permanent damages and deaths (BRENNAN, 1991). From these two studies, it was estimated that around 98,000 North-Americans die every year due to mistakes associated to health care assistance, these being considered one of the leading causes of death in the United States (LEAPE, 1991).

Discussion and interest around medication error are increasing in Brazil, and there is already a considerable number of publications that show the important dimension of AE in Brazilian institutions. Human error study is recent and the health care system is very late in applying this new knowledge, the science of safety, that has some excellence models, such as aviation and nuclear energy generating companies (HELMREICH, 2000). Regardless of this delay, the formation of professionals that deal with human lives is strongly marked by the search for infallibility.

Financial costs of adverse events, in terms of additional treatment and increase in days at the hospital, are considerable. One of the most consistent findings of record reviews is that, on average, a patient suffering from an AE remains from six to eight additional days at the hospital. When sums are performed and findings extrapolated to national level, costs are expressive (VINCENT, 2010).

In England, the cost of avoidable adverse events is 1 million pounds per year only in days lost with hospitalization. Additional costs with lost working time, disablement benefits and other economic consequences are even bigger. The United States of America (USA) Medicine Institute's report estimated that avoidable medical errors result in total costs (including expenses with additional care caused by errors, revenue loss, domestic production and disablement) between 17 and 29 billions of dollars per year at hospitals in the USA.

Prevention of AE may result in budget economy for health institutions. In case of severe complications that require treatment for several hospitalization days, a hospital may have an approximate cost between 7,556 and 56,670 dollars per case (VINCENT, 2010).

3. Patient Safety – Quality in interdisciplinary assistance

Patients that use health care services are susceptible to the occurrence of AE, many times by avoidable, unintentional errors, by professionals that maybe do not master the quality and safety policies defined or by not being properly trained to perform their activities. Such facts may incur in patient damages, resulting, for example,

in prolonged hospitalization period due to infection or a more severe clinical denouement, even with the possibility of obit.

According to the World Health Organization (WHO, 2009), damaged provoked by lack of quality in assistance can be disabling, with permanent sequelae, aside from elevating stay cost, possibly leading to premature death as direct consequence of an unsafe health care practice. This may occur even with quality culture, when patients are exposed to unintentional human errors resulting from drug prescription error, or error on its administration or, still, lack of communication/monitoring of health treatment period.

Patient safety can be understood, according to Vincent (2010), as the act of avoiding, preventing and improving the adverse results or injuries originated in the process of hospital medical assistance. And this expression “patient safety”, by the lack of clarity regarding its applications, is confused with assistance quality.

In this perspective, the Institute of Medicine (IOM, 1999) refers to quality as the degree in which provided services decrease the probability of unfavorable results to the patient and, consequently, increase the probability of favorable results, according to scientific basis. Thus, in order for Health Care assistance quality to exist, it is necessary for safety to be its main pillar.

According to Passos (2013), the movement for security had its start at the end of the 20th century, after the publication of the IOM report, in the USA in 2000, entitled “To Err is Human: building a safety health system”. This study reported in a systematized way the problems that affected patient safety. The study’s statistics showed that, from 33.6 million hospitalizations, 44,000 to 98,000 patients would have died as a result of errors related to the assistance provided by health care teams and that, regarding the errors committed in the health care system, the cost of reparation was estimated up to 29 billions of dollars per year.

Quality, before it was studied and understood in its completeness, was merely thought as the motivation from professionals, that this way would produce quality. It was not thought that bad quality could, for example, be linked to poorly developed structures and processes of hospital assistance, according to Vincent (2010).

There is a direct relationship between quality and safety. In order for assistance to be considered of quality, Passos (2013) states that it is extremely necessary that it is a safe assistance. In this context, he continues to state that the health care professional must master the professional context in which he or she is inserted and, in case there is lack of knowledge around this system, he or she must obtain information from someone who knows best about it in order to ensure the quality-safety binomial.

It is important to make clear that the aforementioned IOM report (1999), states that the problem is not in the existence of incompetent professionals in the health care system, but really, in the fact that there are good professionals working in inadequate systems, which need to be safer to the patients. Vincent (2010) states that the publication of this report was a great stimulus for the development of patient safety, making it part of the pillars of public and political attention in the USA.

Corroborating the IOM report and with other research sources and statistical surveys produced at the National Patient Safety Agency (NPSA), in England, the WHO (2009) established the concept, largely broadcast nowadays, of patient safety that consists in the risk reduction of unnecessary damages associated to health care assistance to an acceptable minimum. The acceptable minimum means what is viable observing current knowledge, available resources and the context in which assistance is provided before the risk of non-treatment or choice for another treatment.

Far beyond the afore described, it possible to comprehend, according to the US National Patient Safety Foundation (USNPSF, 2000) that safety related to patient assistance, emerges from a system’s components interaction, whichever it may be, being more than the act of preventing the occurrence of recognizable or avoidable errors or issues. It is related to assistance quality, however, these should not be viewed as equal concepts.

Nieva (2003) holds the fact that the existence of a consensus around the organization cultural attributes really contribute to patient safety, with these being: decrease in errors, teamwork integration, support of leadership related to the assistance and communication process.

CONCLUSION

The initiatives for orthopedic patient safety promotion in anticoagulant therapy are essential to stop or minimize possible damages to the user’s health.

The present integrative review allowed for the synthesis of what has been produced around the subject of anticoagulant therapy and orthopedics patient safety on health care assistance management in the last 10 years.

With the results of this study, some form of contribution to the discussions about orthopedics patient safety and stimulus to the realization of initiatives by health care professionals is expected, in search for the promotion of the health care assistance quality and Orthopedics patient safety binomial.

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